

NEW
ARIA UPDATE

ARIA

At-A-Glance Pocket Reference

2007

1st Edition



**BASED ON THE ALLERGIC RHINITIS AND ITS IMPACT ON ASTHMA
WORKSHOP REPORT**

*In collaboration with the World Health Organisation,
GA²LEN, and Allergen*

ARIA UPDATE

In 1999, during the ARIA (Allergic Rhinitis and its Impact on Asthma) WHO workshop, an evidence-based document was produced using an extensive review of the literature available up to December 1999. The statements of evidence for the development of ARIA have followed WHO rules and were based on those of Shekelle. ARIA proposed a new classification for allergic rhinitis which was subdivided into “intermittent” or “persistent” disease, and based on severity according to quality-of-life and symptoms. Another important aspect of ARIA was to consider co-morbidities of allergic rhinitis, particularly asthma.

The ARIA document was intended to be a state-of-the-art textbook for the specialist as well as for the general practitioner and other health care professionals:

- To update their knowledge of allergic rhinitis.
- To highlight the impact of allergic rhinitis on asthma.
- To provide an evidence-based documented approach to diagnosis.
- To provide an evidence-based approach to treatment.
- To propose a stepwise approach to the management of the disease.

The ARIA update was started in 2004. Several chapters of ARIA were extensively reviewed using the Shekelle evidence-based model, and papers published in peer-reviewed journals on the topics of: tertiary prevention of allergy, complementary and alternative medicine, pharmacotherapy and anti-IgE treatment, allergen-specific immunotherapy, links between rhinitis and asthma, and mechanisms of rhinitis. There was a need for a global document which would highlight the interactions between the upper and the lower airways including diagnosis, epidemiology, common risk factors, management, and prevention.

A large list of treatments was considered. Concerning pharmacologic treatments, intranasal corticosteroids are the first-line therapy in patients with moderate to severe disease, H1-antihistamines are important treatments for all patients, and leukotriene receptor antagonists (LTRAs) are particularly important for patients with both rhinitis and asthma. Sublingual specific immunotherapy (SIT) has proven to be a safe and effective treatment.

Allergic rhinitis is a symptomatic disorder of the nose induced after allergen exposure due to an IgE-mediated inflammation of the membranes lining the nose. It was defined in 1929 as follows: “The three cardinal symptoms in nasal reactions occurring in allergy are sneezing, nasal obstruction and mucous discharge.”

Allergic rhinitis is a global health problem. Patients from all countries, all ethnic groups, and all ages suffer from allergic rhinitis. Over 500 million patients suffer from this disease. Allergic rhinitis causes major illness and disability worldwide. The prevalence of diagnosed asthma in patients with allergic rhinitis increases as a function of the persistence and severity of rhinitis. Allergic rhinitis causes impairment of sleep, daily activities, and work and can increase the severity of concurrent asthma. The economic impact of allergic rhinitis is substantial.

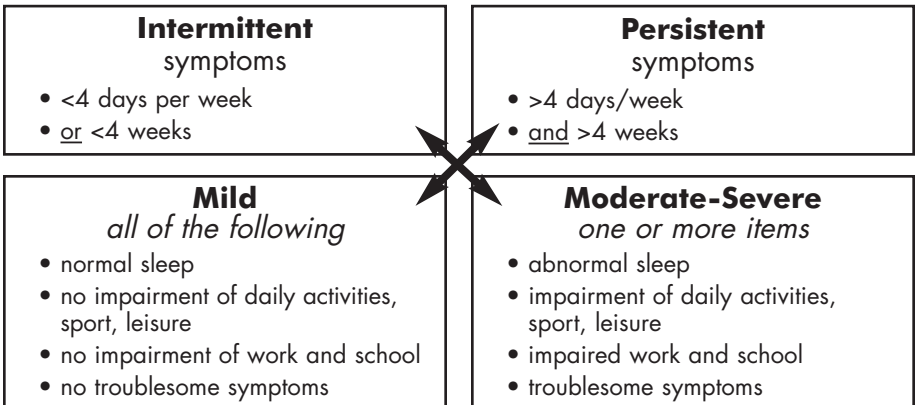
The diagnosis of allergic rhinitis is often easy, but in some cases it may cause problems and many patients go undiagnosed, often because they do not perceive the symptoms of rhinitis as a disease.

ARIA RECOMMENDATIONS

- 1- Allergic rhinitis is a major chronic respiratory disease due to its:
 - Prevalence
 - Impact on quality-of-life
 - Impact on work/school performance and productivity
 - Economic burden
 - Links with asthma
- 2- In addition, allergic rhinitis is associated with sinusitis and other co-morbidities such as conjunctivitis.
- 3- Allergic rhinitis should be considered as a risk factor for asthma along with other known risk factors.
- 4- A new subdivision of allergic rhinitis has been proposed:
 - Intermittent (IAR)
 - Persistent (PER)
- 5- The severity of allergic rhinitis has been classified as “mild” or “moderate/severe” depending on the severity of symptoms and quality-of-life outcomes.
- 6- Depending on the subdivision and severity of allergic rhinitis, a stepwise therapeutic approach has been proposed.
- 7- The treatment of allergic rhinitis combines:
 - Allergen avoidance (when possible)
 - Pharmacotherapy
 - Immunotherapy
 - Education
- 8- Patients with persistent allergic rhinitis should be evaluated for asthma by means of a medical history, chest examination, and, if possible and when necessary, the assessment of airflow obstruction before and after bronchodilator.
- 9- Patients with asthma should be appropriately evaluated (history and physical examination) for rhinitis.
- 10- Ideally, a combined strategy should be used to treat the upper and lower airway diseases to optimize efficacy and safety.

ARIA CLASSIFICATION OF RHINITIS

Proper diagnosis and classification of patients with allergic rhinitis are essential to initiate proper treatment. The symptoms of allergic rhinitis include rhinorrhea, nasal obstruction, nasal itching, and sneezing, which are reversible spontaneously or with treatment.



STRENGTH OF EVIDENCE FOR EFFICACY OF RHINITIS TREATMENT

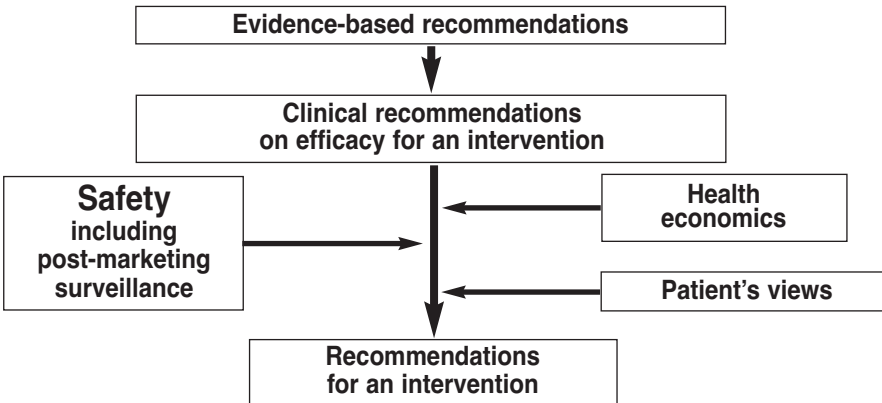
ARIA 2007					
Intervention	SAR		PAR		PER
	adults	children	adults	children	
Oral H1 Antihistamine	A	A	A	A	A
Intranasal H1 Antihistamine	A	A	A	A	A**
Intranasal CS	A	A	A	A	A**
Intranasal cromone	A	A (>12 yrs)	A	A	
LTRAs	A	A	A		A**
Subcutaneous SIT	A	A	A	A	A**
Sublingual / nasal SIT	A	A	A	B	A**
Allergen avoidance	D	D	A*	B*	

SAR - Seasonal Allergic Rhinitis
 PAR - Perennial Allergic Rhinitis
 PER - Persistent Allergic Rhinitis

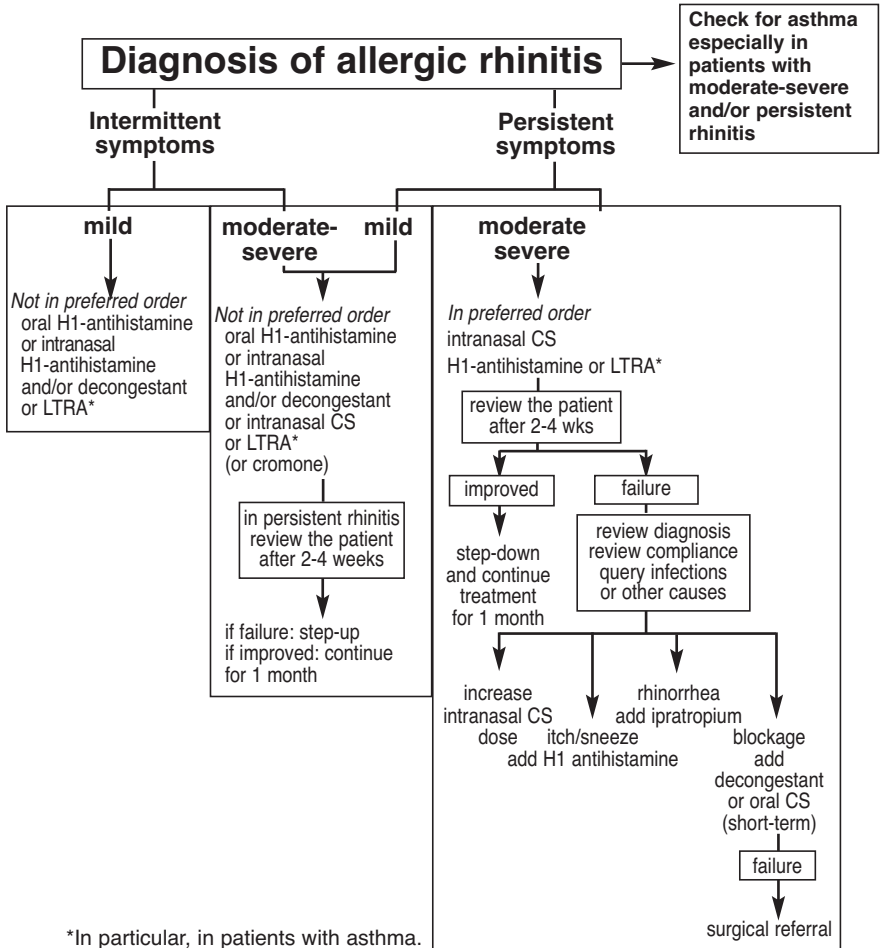
*not effective in the general population
 **extrapolated from studies in SAR/PAR

EVIDENCE-BASED RECOMMENDATIONS

The strength of evidence based on efficacy alone is insufficient to determine proper treatment. The new GRADE classification considers additional factors as indicated in the figure shown below and provides important new information about the quality of clinical information used to make therapeutic decisions. This 1st Edition of the ARIA Pocket Reference reflects the ARIA 2007 Workshop Report. An expert panel meeting was conducted on June 20, 2007; the panel made 48 clinical recommendations based on the GRADE methodology. Following final review, these recommendations will be published later in 2007.



ALGORITHM FOR ALLERGIC RHINITIS DIAGNOSIS AND MANAGEMENT



Allergen and irritant avoidance may be appropriate

If conjunctivitis add:
oral H1-antihistamine
or intraocular H1-antihistamine
or intraocular cromone
(or saline)

Consider specific immunotherapy

GLOSSARY OF RHINITIS MEDICATIONS

Name and Also known as	Generic name	Mechanism of action	Side effects	Comments
Oral H1 antihistamines	2nd generation Acrivastin Azelastine Cetirizine Desloratadine Ebastine Fexofenadine Levocetirizine Loratadine Mequitazine Mizolastine Rupatadine 1st generation Chlorpheniramine Clemastine Dimethindene Hydroxyzine Ketotifen Oxatamine <i>Others</i> Cardiotoxic* Astemizole Terfenadine	<ul style="list-style-type: none"> - new generation drugs can be used once daily - no development of tachyphylaxis 	No cardiotoxicity <ul style="list-style-type: none"> - Acrivastine has sedative effects - Mequitazine has anticholinergic effect - Oral azelastine may induce sedation and a bitter taste 1st generation <ul style="list-style-type: none"> - Sedation is common - And/or anti-cholinergic effect 	Efficacy/safety ratio and pharmacokinetics Rapidly effective (less than 1 hr) on nasal and ocular symptoms Moderately effective on nasal congestion * Cardiotoxic drugs are no longer marketed in most countries
Local H1 antihistamines (intranasal, intraocular)	Azelastine Levocabastine Olopatadine	<ul style="list-style-type: none"> - blockage of H₁ receptor - some anti-allergic activity for azelastine 	<ul style="list-style-type: none"> - Minor local side effects - Azelastine: bitter taste 	Rapidly effective (less than 30 min) on nasal or ocular symptoms
Intranasal glucocorticosteroids	Beclomethasone dipropionate Budesonide Ciclesonide Flunisolide Fluticasone propionate Fluticasone furoate Mometasone furoate Triamcinolone acetonide	<ul style="list-style-type: none"> - potentially reduce nasal inflammation - reduce nasal hyperreactivity 	<ul style="list-style-type: none"> - Minor local side effects - Wide margin for systemic side effects - Growth concerns with BDP only - In young children consider the combination of intranasal and inhaled drugs 	The most effective pharmacologic treatment of allergic rhinitis Effective on nasal congestion Effective on smell Effect observed after 12 hr but maximal effect after a few days
Oral / IM glucocorticosteroids	Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone	<ul style="list-style-type: none"> - Potently reduce nasal inflammation - Reduce nasal hyperreactivity 	<ul style="list-style-type: none"> - Systemic side effects common in particular for IM drugs - Depot injections may cause local tissue atrophy 	When possible, intranasal glucocorticosteroids should replace oral or IM drugs However, a short course of oral glucocorticosteroids may be needed if moderate/severe symptoms

Name and Also known as	Generic name	Mechanism of action	Side effects	Comments
Local cromones (intranasal, intraocular)	Cromoglycate Nedocromil Naaga	- mechanism of action poorly known	- Minor local side effects	Intraocular cromones are very effective Intranasal cromones are less effective and their effect is short lasting Overall excellent safety
Oral decongestants	Ephedrine Phenylephrine Phenyl- propranolamine Pseudoephedrine Oral H1- antihistamine- decongestant combination	- sympathomimetic drugs - relieve symptoms of nasal congestion	- Hypertension - Palpitations - Restlessness - Agitation - Tremor - Insomnia - Headache - Dry mucous membranes - Urinary retention - Exacerbation of glaucoma or thyrotoxicosis	Use oral decongestants with caution in patients with heart disease Oral H1-antihistamine decongestant combination products may be more effective than either product alone but side effects are combined
Intranasal decongestants	Oxymethazoline <i>Others</i>	- sympathomimetic drugs - relieve symptoms of nasal congestion	- Same side effects as oral decongestants but less intense - Rhinitis medicamentosa is a rebound phenomenon occurring with prolonged use (over 10 days)	Act more rapidly and more effectively than oral decongestants Limit duration of treatment to less than 10 days to avoid rhinitis medicamentosa
Intranasal anti-cholinergics	Ipratropium	- anticholinergics block almost exclusively rhinorrhea	- Minor local side effects - Almost no systemic anticholinergic activity	Effective on allergic and nonallergic patients with rhinorrhea
CysLT antagonists	Montelukast Pranlukast Zafirlukast	- Block CysLT receptor	- Excellent tolerance	Effective on rhinitis and asthma Effective on all symptoms of rhinitis and on ocular symptoms

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Adapted from the 2007 ARIA Workshop Report.
ARIA source documents are at www.whiar.org
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